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L17: Entry 4 of 6 File: USPT Jul 10, 2001

DOCUMENT-IDENTIFIER: US 6258597 B1
TITLE: Stimulation of hematopoietic cells in vitro

Brief Summary Text (13):
As used herein, an inhibitor of dipeptidyl peptidase type IV ("DPIV") generally refers to a molecule which inhibits the functional activity of the DPIV. Accordingly, the inhibitors of the invention include inhibitors of the enzymatic activity of the dipeptidyl peptidase type IV. Preferably, the inhibitors of the enzymatic activity of DPIV associate with the active site of DPIV by covalently bonding thereto or by forming an ionic interaction therewith. Such inhibitors include competitive inhibitors of DPIV, such as transition state analogs of DPIV, and non-competitive inhibitors of DPIV, such as fluoroalkylketones. Inhibitors of DPIV also include non-competitive inhibitors of DPIV which selectively bind to DPIV (covalently or via ionic interactions) at a site on the DPIV protein other than the active site and, thereby, inhibit the enzymatic activity of the DPIV. Such non-competitive inhibitors are one category of binding molecules which selectively bind to DPIV and have the ability to stimulate hematopoietic cells or thymocytes in vitro. Other binding molecules which selectively bind to DPIV and have the ability to stimulate hematopoietic cells include monoclonal antibodies, polyclonal antibodies and fragments of the foregoing which are capable of: (1) binding to DPIV, and (2) stimulating hematopoietic cells and/or thymocytes in vitro. The inhibitors of DPIV that are useful in the context of the present invention may be immobilized or insoluble form. In general, the foregoing inhibitors can be monovalent, bivalent, or multivalent. (See e.g., U.S. Ser. Nos. 08/671,756 and 08/837,305, entitled "Multivalent Compounds for Crosslinking Receptors and Uses Thereof" for a description of dimers and other conjugates of DPIV inhibitors.) The immobilized DPIV inhibitor may be immobilized to a variety of immobilization structures including conventional culture vessels (e.g., stirring flasks, stirred tank reactors, air lift reactors, suspension cell reactors, cell adsorption reactors and cell entrapment reactors, petri dishes, multi well plates, micro titer plates, test tubes, culture flasks, bags and hollow fiber devices, and cell foam. Such immobilization structures preferably are formed of materials including, for example, polystyrene, polypropylene, acrylate polymers, nylon, cloth, nitrocellulose, agarose, sepharose, and so forth.

Other Reference Publication (53):
Duke-Cohan, J.S., et al., "Targeting of an Activated T-Cell Subset Using a Bispecific Antibody-Toxin Conjugatedirected Against CD4 and CD26", Blood, (1993), 82:2224-2234. (Abstract Only).

Other Reference Publication (63):
Barton, R.W.J., et al., "Binding Of The T Cell Activation Monoclonal Antibody Tal To Dipeptidyl Peptidase IV", J. Of Leukocyte Biology 48:291-296 (1990). Abstract Only.

Other Reference Publication (74):
Schon, E., et al., "The Role Of Dipeptidyl Peptidase IV In Human T Lymphocyte Activation. Inhibitors And Antibodies Against Dipeptidyl Peptidase IV Suppress Lymphocyte Proliferation And Immunoglobulin Synthesis In Vitro", Eur. J. Of Immunol. 17:1821-1826 (1987). Abstract Only.